

CLAIMS

I Claim:

1. An implantable sensor for sensing a concentration of an organic substrate, the sensor comprising:
  2. a conductive electrode; and
  3. a stabilized enzyme emulsion in contact with the electrode, the enzyme emulsion comprising:
    4. an enzyme that quantitatively oxidizes the organic substrate;
    5. a water immiscible oxygen dissolving compound emulsified into intimate contact with the enzyme to provide oxygen; and
    6. a protein crosslinking agent to crosslink and insolubilize the enzyme forming a stabilized gel comprising crosslinked protein and particles of the oxygen dissolving substance.
1. The implantable sensor of Claim 1 further comprising a semipermeable membrane covering the electrode with the enzyme emulsion sandwiched between the membrane and the electrode.
1. The implantable sensor of Claim 1, wherein the enzyme emulsion 2. also contains an additional carrier protein.

1           4. The implantable sensor of Claim 3, wherein the additional carrier  
2   protein is selected from the group consisting of serum albumin and, gelatin.

1           5. The implantable sensor of Claim 1, wherein the oxygen dissolving  
2   substance is selected from the group consisting of perfluorocarbons, silicone oils,  
3   fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and  
4   steroids.

1           6. The implantable sensor of Claim 5, wherein the oxygen dissolving  
2   substance is a perfluorocarbon liquid selected from the group consisting of perfluoroctyl  
3   bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluoro-  
4   phenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoro-  
5   methyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluoro-  
6   trimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluoro-  
7   diisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane, perfluoro-  
8   dimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1           7. The implantable sensor of Claim 1, wherein the crosslinking agent  
2   is selected from the group consisting of aldehydes, carbodiimides, imidoesters,  
3   pyrocarbonates, epoxides and N-hydroxysuccinimid esters.

1           8. The implantable sensor of Claim 1, wherein the oxidase enzyme is  
2 selected from the group consisting of cholesterol oxidase, amino acid oxidase, alcohol  
3 oxidase, lactic acid oxidase, oxygen oxidoreductase, galactose oxidase, and glucose  
4 oxidase.

1           9. The implantable glucose sensor of Claim 1 further comprising an  
2 electron transport compound dissolved in the perfluorocarbon liquid.

1           10. The implantable glucose sensor of Claim 9, wherein the electron  
2 transport compound comprises ferrocene.

1           11. The implantable sensor of Claim 1, wherein the enzyme emulsion  
2 further comprises an antioxidant.

1           12. The implantable sensor of Claim 1, wherein the enzyme emulsion  
2 further comprises an antimicrobial agent.

1           13. The implantable sensor of Claim 1, wherein the enzyme emulsion  
2 further comprises an anti-inflammatory agent selected from the group consisting of  
3 steroids, lymphokines, and non-steroidal anti-inflammatory drugs.

1                   14. An implantable glucose sensor for sensing a concentration of  
2 glucose, the sensor comprising:  
3                   a metal electrode; and  
4                   a stabilized enzyme emulsion in contact with the electrode, the enzyme  
5                   emulsion comprising:  
6                   a solution of glucose oxidase protein for oxidizing glucose to  
7                   quantitatively produce hydrogen peroxide;  
8                   a perfluorocarbon liquid emulsified with the glucose oxidase; and  
9                   a crosslinking agent to crosslink covalently said protein to form a  
10                  stabilized gel comprising crosslinked protein and particles of the  
11                  perfluorocarbon liquid.

1                   15. The implantable glucose sensor of Claim 14 further comprising a  
2 semipermeable membrane covering the electrode with the enzyme emulsion in contact  
3 with a first surface of the membrane and sandwiched between the membrane and the  
4 electrode and with body fluids or cells in contact with a second surface of the semi-  
5 permeable membrane.

1                   16. The implantable sensor of Claim 14, wherein the oxygen  
2 dissolving substance is selected from the group consisting of perfluorocarbons, silicone  
3 oils, fluorosilicone oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids  
4 and steroids.

1           17. The implantable sensor of Claim 16, wherein the oxygen  
2   dissolving substance is a perfluorocarbon liquid selected from the group consisting of  
3   perfluoroctyl bromide, perfluorodichlorooctane, perfluorodecalin, perfluoroindane,  
4   perfluorophenanthrene, perfluorotetramethylcyclohexane, perfluoropolyalkylether oil,  
5   perfluoromethyldecalin, perfluorodimethylethylcyclohexane, perfluorodimethyldecalin,  
6   perfluorotrimethyldecalin, perfluoroisopropyldecalin, perfluoropentamethyldecalin,  
7   perfluorodiisopropyl decalin, perfluorodiethyldecalin, perfluoromethyladamantane,  
8   perfluorodimethyladamantane, perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1           18. The implantable glucose sensor of Claim 14 further comprising an  
2   electron transport compound dissolved in the perfluorocarbon liquid.

1           19. The implantable glucose sensor of Claim 18, wherein the electron  
2   transport compound comprises ferrocene.

1           20.    A method for producing a stabilized enzyme emulsion for use with  
2    a polarographic or amperometric sensor comprising the steps of:  
3               making an aqueous solution of a water soluble enzyme that oxidizes an  
4               organic substrate to produce hydrogen peroxide;  
5               emulsifying a volume of a water immiscible oxygen dissolving substance  
6               into the aqueous solution to form an emulsion;  
7               contacting the emulsion with a protein crosslinking agent; and  
8               spreading a mixture of the protein crosslinking agent and the emulsion  
9               into a uniform layer whereby the emulsion becomes crosslinked to  
10              form a solid gel.

1           21.    The method of Claim 20, wherein to the emulsion is contacted with  
2    a carrier protein prior to contacting with the protein crosslinking agent.

1           22.    The method of Claim 21, wherein the aqueous solution contains  
2    the carrier protein and the water soluble enzyme is added to the emulsion prior to  
3    contacting with the protein crosslinking agent.

1           23.    The method of Claim 20, wherein the oxygen dissolving substance  
2    is selected from the group consisting of perfluorocarbons, silicone oils, fluorosilicone  
3    oils, aromatic and aliphatic hydrocarbon oils or solids, carotenoids and steroids.

1                   24. The method of Claim 23, wherein the oxygen dissolving substance  
2    is a perfluorocarbon liquid selected from the group consisting of perfluoroctyl bromide,  
3    perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,  
4    perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,  
5    perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,  
6    perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,  
7    perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,  
8    perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.

1                   25. A method for producing a stabilized enzyme emulsion for use with  
2    a polarographic sensor comprising the steps of:  
3                   making an aqueous solution of a carrier protein;  
4                   emulsifying a volume of a perfluorocarbon liquid into the aqueous  
5                   solution to form an emulsion;  
6                   contacting the emulsion with a water soluble enzyme that oxidizes an  
7                   organic substrate to produce hydrogen peroxide to form a mixture;  
8                   contacting the mixture with a protein crosslinking agent; and  
9                   spreading a mixture of the protein crosslinking agent and the emulsion  
10                   into a uniform layer whereby the emulsion becomes crosslinked to  
11                   form a solid gel.

1                   26. The method of Claim 25, wherein the oxygen dissolving substance  
2                   is a perfluorocarbon liquid selected from the group consisting of perfluorooctyl bromide,  
3                   perfluorodichlorooctane, perfluorodecalin, perfluoroindane, perfluorophenanthrene,  
4                   perfluorotetramethylcyclohexane, perfluoropolyalkylether oil, perfluoromethyldecalin,  
5                   perfluorodimethylethylcyclohexane, perfluorodimethyldecalin, perfluorotrimethyldecalin,  
6                   perfluoroisopropyldecalin, perfluoropentamethyldecalin, perfluorodiisopropyl decalin,  
7                   perfluorodiethyldecalin, perfluoromethyladamantane, perfluorodimethyladamantane,  
8                   perfluoro-di-xylethane, and perfluoro-6,7 H-undec-6-ene.